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| EXAMINER | |
|---|---|
| PIHONAK, SARAH | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/528,437 | MAGAR ET AL. | |
| | Examiner | Art Unit | |
| | SARAH PIHONAK | 4121 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-32,34 and 35* is/are pending in the application.

4a) Of the above claim(s) *1-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-32,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

This application is a 371 (national stage application) of PCT/EP03/50640, filed on 9/19/03, and claims priority to Provisional Application No. 60/412308, filed on 9/20/02.

***Priority***

This application claims priority to Provisional Application No. 60/412308, filed on 9/20/02. The effective filing date of the instant application is 3/18/05. As the provisional application provides support to the instant claims, the priority date given to the instant claims is 9/20/02.

1. Claims 1-32, and 34-35 are pending.

2. Applicant's election without traverse of the invention of Group I, claims 23-32, 34-35 in the reply filed on 2/27/09 is acknowledged. The Examiner also acknowledges the species election, without traverse, of the following compound: 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide.

3. Claims 1-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/27/09.

4. Claims 23-32, and 34-35 were examined.

5. Claims 23-32, and 34-35 are rejected.

***35 U.S.C. § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

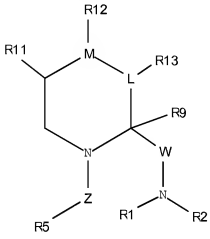
7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 23-32, and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 00/08015 publication, in view of Patani et. al., *Chemical Rev.*, **96**, 1996, pp. 3147-3176. The WO 00/08015 publication was submitted by the Applicants in the Information Disclosure Statements submitted on 6/29/06.

9. Instant claim 23 cites a compound of Formula (I), of which the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, is a species. The '015 publication teaches that compounds of Formula VI below can be prepared:

Formula IX




Where L and M = CH, N, O, S (but not both heteroatoms) (p. 7, lines 1-12);

W = (C=O), (NH(C=O)), (NH(C=O)CH2), (C=NH), (C=S), SO2, CH2, or methylene substituted with one or more substituents (p. 3, lines 27-29);

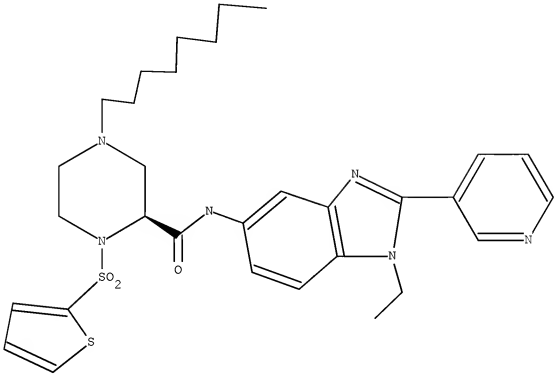
Z = (C=O), (NH), (C=N), SO2, or (C=O)NH, etc. (p. 4, lines 3-5);

R1 and R5 = H, C-10 alkyl, aryl, C3-7 heterocycle, etc. (p. 3, lines 9-19);

R2 = H, C1-6 alkyl, aryl, aryl substituted with one or more substituents, aryl groups fused with other aryl groups, heterocycles, etc. (p. 3, lines 20-26);

R9, R11, R12, R13 = H, C1-8 alkyl, etc. (p. 7, lines 7-9, p. 4, lines 21-23, and p. 5, lines 1-8).

The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, is shown below:



The '015 publication teaches that for Formula IX, M may be N (p. 7, lines 1-11), and that Z may be S(O)2 (p. 7, line 6, p. 4, line 3). The '015 publication also teaches that W may be carbonyl (p. 3, line 27), and that R1, R11, R13, and R9 may be H (p. 7, lines 1-9, p. 4, lines 20-22, and p. 3, line 9). Additionally, the '015 publication discloses that L may be CH (p. 7, line 11), and R2 may be aryl, heteroaryl, aryl groups substituted with one or more substituents, and aryl groups that are fused with other aromatic groups, heterocycles (p. 3, lines 20-26); R5 may be an aryl group (p. 3, lines 9 and 16); R12 may be C1-8 alkyl (p. 4, lines 20-22, and p. 7, line 7). The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at the corresponding R5 position of formula IX; the thienyl group is a heteroaryl group. The elected compound also has a 1-

octyl substituent at the corresponding R12 position of formula IX; the Z position is SO2, M is N, and L is CH; R11, R9, and R13 are H; R1 is H, and R2 is the substituted benzoimidazol group, which is an phenyl group fused with a heterocycle substituted with a pyridine group and an ethyl group. Therefore, the '015 publication discloses compounds that are very similar to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. The only difference between the compounds of formula IX disclosed by the WO '015 publication and the elected compound is that, for compounds of formula IX, the R5 substituent may be aryl, while the elected compound has a thienyl group at this position, which is a heteroaryl group.

10. Instant claim 24 cites the compound as stated in instant claim 23, and also, that the R2 position is either aryl, heteroaryl, 3-8 membered cycloalkyl, or heterocycloalkyl. The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, which is a species of this claim, has a phenyl ring which is fused with a substituted heterocycle. The '015 publication teaches that the R2 position may be occupied by aryl groups that are fused with substituted heterocycles (p. 3, lines 20-26, and p. 7, lines 1-6).

11. Instant claim 25 cites the compound as stated in instant claim 23, and also, that the R4 substituent is either C1-6 alkyl, C1-6 alkyl amino, aryl, heteroaryl, 3-8 membered cycloalkyl or heterocycloalkyl. The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at the R4 position. The '015 publication teaches that this substituent,

which corresponds to the R5 position of formula IX, may be occupied by an aryl group (p. 3, lines 9 and 16, and p. 7, lines 1-6). The thienyl group is a heteroaryl group.

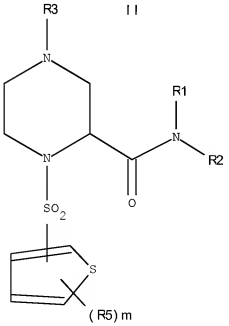
12. Instant claim 26 cites the compound as stated in instant claim 23, and additionally, that the groups are defined as follows: R2 is aryl, R3 is either C1-8 alkyl, C1-8 acyl amino, C1-8 alkyl acyl, and R4 is either C1-6 alkyl, amino aryl, or heteroaryl. The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has the R2, R3, and R4 groups stated as follows: R2 is substituted benzoimidazol (aryl), R3 is octyl, and R4 is thienyl. Regarding compounds of formula IX, the R2 group corresponds to the R2 group for the instant claim, the R12 group corresponds to the R3 position for the instant claim, and the R5 group corresponds to the R4 group in the instant claim. The '015 publication teaches that the R2 position for compounds of formula IX may be aryl (p. 3, lines 20, 22-23, and p. 7, lines 1-6); the R12 group may be C1-8 alkyl (p. 4, lines 20 and 22, and p. 7, lines 1-8); the R5 group may be aryl, or a C3-7 heterocycle, etc. (p. 3, lines 9-19, p. 7, lines 1-6). The thienyl group is a heteroaryl group. Therefore, the '015 publication teaches compounds that are very similar to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. The only difference between the elected compound and the compounds taught by the WO '015 publication is that the R5 group for formula IX is an aryl group (p. 3, lines 9 and 16, p. 7, lines 1-6).

13. Instant claim 27 cites the compound as stated in instant claim 23, and furthermore, that the R2 substituent is a fused phenyl group. The elected compound, 4-

octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has the substituted benzoimidazol group at the R2 position. The '015 publication also discloses that the R2 position for compounds of formula IX may be phenyl group fused with substituted heterocyclic groups, or aromatic groups (p. 3, lines 20-26, and p. 7, lines 1-6).

14. Instant claim 28 cites the compound as stated in instant claim 23, and that the R4 substituent is thienyl. The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at the R4 position. The '015 publication teaches that for compounds of formula IX, the R5 substituent, which corresponds to the R4 position for the instant claim, may be a heterocycle (p. 3, lines 9 and 17, and p. 7, lines 1-6).

15. Instant claim 29 cites the compound as stated in instant claim 23, and also, that the compound has the following formula II shown below:



For the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, the substituents are defined as follows: R3=1-octyl, R1=H, R2= 1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl, and m=0. The '015 publication teaches that for compounds of formula IX, the R12 group, which corresponds to the R3 position of the instant claim, may be C1-8 alkyl (p. 4, lines 20 and 22, and p. 7, lines 1-7), and that the R1 group, which corresponds to the same R1 group of the instant claim, may be H (p. 3, line 9, and p. 7, lines 1-6). The '015 publication also discloses that R2, which corresponds to the R2 group of the instant claim, may be a fused, substituted phenyl group, such as 1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl (p. 3, lines 20-26, and p. 7, lines 1-6). The '015 publication also teaches that the group substituent attached to the sulfonyl group, which corresponds to position R5 of formula IX, may be an aryl group (p. 3, lines 9 and 16, and p. 7, lines 1-6). The thienyl group is a heteroaryl group.

16. Instant claim 30 cites the compound as stated in instant claim 23, and furthermore, that the R2 position is carbazoyl, tetrahydro-beta-carbolinyl, or benzoimidazol. For the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, the R2 substituent is benzoimidazol. The '015 publication also teaches that the R2 position of compounds of formula IX may be a substituted fused phenyl group (p. 3, lines 20-26, and p. 7, lines 1-6), of which benzoimidazol is.

17. Instant claim 31 cites the compound as stated in instant claim 23, and also, that the compound is selected from a list of specific compounds, one of which is the elected

compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. The '015 publication discloses compounds of formula IX that are very similar to the elected compound (p. 3, lines 1-29, p. 4, lines 1-6, and lines 20-22, p. 7, lines 1-12). The difference between the compounds of formula IX and the elected compound is that for the R5 position of formula IX, the substituent may be an aryl group (p. 3, lines 9 and 16, and p. 7, lines 1-12). The elected compound has a thienyl group, which is a heteroaryl group, at this corresponding position.

18. Instant claim 32 cites a pharmaceutical composition comprised of the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. The '015 publication teaches that compounds very similar to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, may be present in a pharmaceutical composition (Abstract, p. 3, lines 1-29, p. 4, lines 1-6, and lines 20-22, p. 7, lines 1-12).

19. Instant claim 34 cites a pharmaceutical composition comprised of the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, in a pharmaceutically acceptable carrier. The '015 publication also discloses that compounds very similar to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, may be present in a pharmaceutically acceptable carrier (p. 3, lines 1-29, p. 4, lines 1-6, and lines 20-22, p. 7, lines 1-12, p. 17, lines 9-11).

20. Instant claim 35 cites the pharmaceutical composition as stated in instant claim 34, and that the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, is packaged together with instructions for use of the elected compound to treat infertility. The '015 publication teaches that the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, may be present in pharmaceutical compositions for the use of treating infertility (Abstract, p. 2, lines 19-22, and p. 3, lines 1-29, p. 4, lines 1-6, and lines 20-22, p. 7, lines 1-12, p. 17, lines 9-11). The '015 publication teaches that compounds very similar to the elected compound are present in a pharmaceutical composition (p. 3, lines 9-29, p. 4, lines 1-5, and p. 7, lines 1-12). As the instant claim is drawn to a composition, the instructions are considered non-functional descriptive matter and were not considered to be pertinent to the patentability of the claim.

21. Regarding instant claim 23, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

22. Regarding instant claim 24, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-

piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

23. Regarding instant claim 25, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

24. Regarding instant claim 26, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

25. Regarding instant claim 27, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

26. Regarding instant claim 28, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

27. Regarding instant claim 29, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

28. Regarding instant claim 30, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

29. Regarding instant claim 31, the WO '015 publication does not teach the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, but does teach compounds that are very similar. The only difference between the elected compound and the compounds of formula IX taught by the WO '015 publication is that for compounds of formula IX, the R5 substituent is an aryl group (p. 3, lines 9 and 16, p. 7, lines 1-12); the corresponding substituent for the elected compound is a thienyl group, which is a heteroaryl group.

30. Regarding instant claim 32, the WO '015 publication teaches every limitation of the claim, with one exception: the R5 substituent of compounds of formula IX is taught as being an aryl group, while the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this position, which is a heteroaryl group.

31. Regarding instant claim 34, the WO '015 publication teaches that compounds very similar to the elected compound are present in a pharmaceutically acceptable carrier (p. 17, lines 9-11).

32. Regarding instant claim 35, the WO '015 publication teaches that compounds very similar to the elected compound are present in a pharmaceutical composition (Abstract, p. 3, lines 9-29, p. 4, lines 1-5, p. 7, lines 1-12).

33. While the WO '015 publication does not teach the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, compounds are disclosed that are very similar to the elected compound, as discussed for instant claim 23. The WO '015 publication teaches compounds of formula IX, as discussed for instant claim 23. The only difference between the compounds disclosed by the WO '015 publication as formula IX and the elected compound is that for the R5 position of formula IX, the substituent may be aryl ( p. 3, lines 9 and 16, and p. 7, lines 1-12); for the elected compound, the corresponding position is occupied by a thienyl group, which is a heteroaryl group. Patani et. al. teaches that benzene, thiophene, and pyridine rings, in relation to biological activity of pharmaceutical compounds, are equivalent bioisosteres of each other (p. 3158, 1st paragraph, titled "Ring Equivalents"). The term bioisostere is used in medicinal chemistry, and is used to define substituents or groups that have similar physical or chemical properties to each other. Patani et. al teaches that bioisosteres provide similar biological activity due to their similar physicochemical properties (p. 3148, 1st full paragraph). Therefore, the substitution of an aryl group for a thienyl group at the R5

position of formula IX would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as the WO '015 publication teaches that compounds of formula IX are useful in compositions for the treatment of infertility, and Patani et. al. teaches that aryl groups such as benzene and a heteroaryl group such as thienyl, or thiophene, are equivalent, in terms of physicochemical properties and biological activity. The elected compound would have been expected, at the time the invention was made, to have the same inherent characteristics as the disclosed compounds of formula IX.

***Rejections-Obviousness Double Patenting***

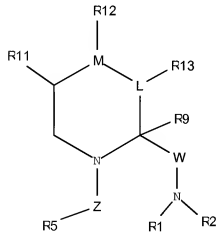
34. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

35. Claims 23-32, and 34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4, 5, and 8 of U.S. Patent No. 6,235,755 in view of WO 00/08015.

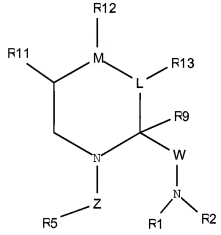
36. Instant claim 23 cites the compound of general formula (I), of which the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, is a species. Claim 4 of US '755 patent cites a compound of formula shown below:



Where M and L are CH; Z=(C=O); W=(C=O); R9, R11, and R13=H, etc.; R1=unsubstituted carbazolyl or carbazolyl substituted with one or more substituents; R2=H; R5=pyran, chromene, or benzofuran; R12=C1-8 alkyl, etc. The compound disclosed in claim 4 of the US '755 patent differs from the elected compound of the instant application by the following functional groups: For the elected compound, M is N; Z=S(O)2; R2, which corresponds to the R1 position of claim 4 of the US '755 patent, is benzoimidazol, rather than carbazolyl, and R4, which corresponds to the R5 position of the compound of claim 4, is thienyl. However, the '015 patent teaches that, in addition to M being N, M may also be CH; Z may also be carbonyl as well as sulfonyl; and that the R5 position, which corresponds to the R4 position of the elected compound, may be occupied by a C3-7 heterocycle, an aryl, or a fused aryl group (p. 3, lines 9-29, p. 4, lines 1-5, and lines 20-22, p. 5, lines 1-8, p. 7, lines 1-12). Additionally, the R1 position, which corresponds to the R2 position for the elected compound and for the formula IX compounds of the '015 publication, may be occupied by a fused aryl group (p. 3, lines 20-26, p. 7, lines 1-6). Thienyl and pyran are both C5 heteroaromatic groups, while chromene is a fused aryl group. As the thienyl and pyran groups are both aromatic groups, the characteristics and properties between the two substituents would not have been expected to be significantly different from each other. Carbazolyl and benzoimidazol are both fused aryl groups. Therefore, the '015 publication teaches that both the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, and the compounds of claim 4 of the US '755 patent are equivalent derivatives of each other.

37. Instant claim 24 cites the elected compound of claim 23, and also, that the R2 group is aryl, heteroaryl, 3-8 membered cycloalkyl, and heterocycloalkyl. For the elected compound, the R2 position is occupied by the substituted benzoimidazol group. Claim 5 of the US '755 patent discloses a compound of the structure shown in claim 4, and also, that the compound has the following functional groups: R9, R11, and R13 are H; R12 may be C1-8 alkyl, and the carbazolyl group may be substituted with the selection of functional groups listed in claim 5. The compound of claim 4 is an equivalent derivative to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, in view of the '015 publication, as discussed for instant claim 23 above. The '015 publication also teaches that the R9, R11, and R13 groups may be H; that the R12 position may be C1-8 alkyl, and that the R2 position, which corresponds to the R1 position of claim 5 of the US '755 patent, may be a fused phenyl group with one or more substituents (p. 3, lines 20-26, p. 4, lines 20-22, and p. 7, lines 1-9). For the elected compound, the R9, R11, and R13 groups are all H; and the R12 group is 1-octyl. While the elected compound has a substituted benzoimidazol group instead of a substituted carbazolyl group, the '015 publication teaches that either functional group may be present, as both the substituted benzoimidazol and substituted carbazolyl substituents are fused phenyl groups. As such, the compounds disclosed in claim 5 of the US '755 patent are equivalent to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, as taught by the '015 publication.

38. Instant claim 25 cites the elected compound, as stated in instant claim 23, and also, that the R4 group may be selected from C1-6 alkyl, C1-6 alkyl amino, aryl, heteroaryl, 3-8 membered cycloalkyl, and heterocycloalkyl. The elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, has a thienyl group at this corresponding position, which is a heteroaryl group as well as a heterocycle. Claim 4 of the US '755 patent discloses a compound of the structure shown below:




Where M and L are CH; Z=(C=O); W=(C=O); R9, R11, and R13=H, etc.; R1=unsubstituted carbazolyl or carbazolyl substituted with one or more substituents; R2=H; R5=pyran, chromene, or benzofuran; R12=C1-8 alkyl, etc. The compound disclosed in claim 4 of the US '755 patent differs from the elected compound of the instant application by the following function groups: For the elected compound, M is N; Z=S(O)2; R2, which corresponds to the R1 position of claim 4 of the US '755 patent, is benzoimidazol, rather than carbazolyl, and R4, which corresponds to the R5 position of

the compound of claim 4, is thienyl. However, the '015 patent teaches that, in addition to M being N, M may also be CH; Z may also be carbonyl as well as sulfonyl; and that the R5 position, which corresponds to the R4 position of the elected compound, may be occupied by a C3-7 heterocycle, or a fused aryl group (p. 3, lines 9-29, p. 4, lines 1-5, and lines 20-22, p. 5, lines 1-8, p. 7, lines 1-12). Additionally, the R1 position, which corresponds to the R2 position for the elected compound and for the formula IX compounds of the '015 publication, may be occupied by a fused aryl group (p. 3, lines 20-26, p. 7, lines 1-6). Thienyl and pyran are both C5 heterocycle, while chromene is a fused aryl group. Carbazolyl and benzoimidazol are both fused aryl groups. Therefore, the '015 publication teaches that both the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, and the compounds of claim 4 of the US '755 patent are equivalent derivatives of each other.

39. Instant claim 26 cites the elected compound as stated in instant claim 23, and also, that R2=aryl; R3=C1-6 alkyl, C1-8 acyl amino, or C1-8 alkyl acyl; R4=C1-6 alkyl, amino aryl, or heteroaryl. For the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, the R2 position is occupied by the benzoimidazol group, which is aryl. Claim 5 of the US '755 patent cites the compound of the general formula as stated in claim 4, and also, that R9, R11, and R13=H; R12=C1-8 alkyl; and that the substituents on the heterocycles, aromatic groups, or other functional groups may be as listed in the claim. The compound of claim 5 differs from the elected compound of the instant application

by the following substituents: For the elected compound, M is N; Z=S(O)2; R2, which corresponds to the R1 position of claim 4 of the US '755 patent, is benzoimidazol, rather than carbazolyl, and R4, which corresponds to the R5 position of the compound of claim 4, is thienyl. However, the '015 patent teaches that, in addition to M being N, M may also be CH; Z may also be carbonyl as well as sulfonyl; and that the R5 position, which corresponds to the R4 position of the elected compound, may be occupied by a C3-7 heterocycle, an aryl, or a fused aryl group (p. 3, lines 9-29, p. 4, lines 1-5, and lines 20-22, p. 5, lines 1-8, p. 7, lines 1-12). Additionally, the R1 position, which corresponds to the R2 position for the elected compound and for the formula IX compounds of the '015 publication, may be occupied by a fused aryl group (p. 3, lines 20-26, p. 7, lines 1-6). Thienyl and pyran are both C5 heteroaromatic groups, while chromene is a fused aryl group. Carbazolyl and benzoimidazol are both fused aryl groups. Additionally, claim 5 of the US '755 patent cites that the carbazolyl, chromene, pyran, and benzofuran groups may be substituted. While the thienyl group of the elected compound does not have any substituents, the '015 publication teaches that the group present at this position, which is the R5 position for formula IX and the R4 position for the elected compound, may be substituted (p. 3, lines 9-19, p. 7, lines 1-6). Therefore, the '015 publication teaches that the compounds as cited in claim 5 of the US '755 patent and the elected compound 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, are equivalent derivatives of each other.

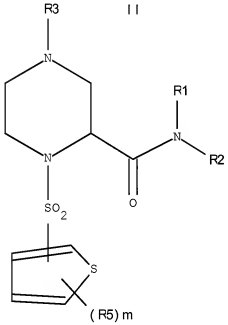
40. Instant claim 27 cites the elected compound as stated in instant claim 23, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-

benzoimidazol-5-yl) amide, and further includes, that the R2 position is a fused phenyl. For the elected compound, the R2 position is occupied by the fused aromatic compound benzoimidazole. Claim 5 of the US '755 patent cites the compound of the general formula as stated in claim 4, and also, that R9, R11, and R13=H; R12=C1-8 alkyl; and that the substituents on the heterocycles, aromatic groups, or other functional groups may be as listed in the claim. While the benzoimidazole and carbazolyl groups are not identical, the '015 publication teaches that this position, which corresponds to the R2 position of formula IX, may be occupied by a fused phenyl group, which may have one or more substituents (p. 3, lines 20-26, p. 7, lines 1-6). The benzoimidazole and carbazolyl groups are both fused phenyl groups. Therefore, the '015 publication teaches that the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, and the compounds as stated in claim 1 of the US '755 patent are equivalent derivatives of each other.

41. Instant claim 28 cites the elected compound as stated in instant claim 23, and that the R4 group is thienyl. For the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, the R4 group is thienyl. Claim 4 of the US '755 patent cites that this position, which corresponds to the R5 position of the stated compound, is occupied by pyran, chromene, or benzopyran, which may be substituted with one or more substituents. While the thienyl, pyran, and chromene groups are not identical, the thienyl and pyran groups are both C5 heteroaromatic groups, while the chromene group is a fused phenyl group. The '015 publication teaches that this corresponding position of formula IX, R5,

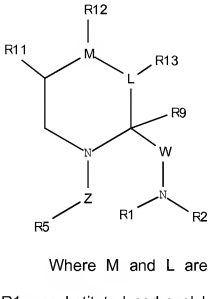
may be occupied by aromatic groups, as well as fused phenyl groups (p. 3, lines 9-19, and p. 7, lines 1-6). As such, the '015 publication teaches that these groups are equivalent to each other.

42. Instant claim 29 cites the compound as stated in instant claim 23, and also, that the compound has the formula II




For the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, the substituents are defined as follows: R3=1-octyl, R1=H, R2= 1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl, and m=0. Claim 4 of the US '755 patent cites that compounds of the formula shown below have the following functional groups:

Formula IX



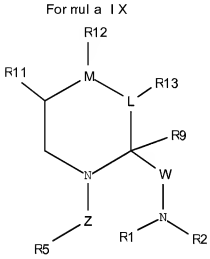

Where M and L are CH; Z=(C=O); W=(C=O); R9, R11, and R13=H, etc.; R1=unsubstituted carbazolyl or carbazolyl substituted with one or more substituents; R2=H; R5=pyran, chromene, or benzofuran; R12=C1-8 alkyl, etc. The compound disclosed in claim 4 of the US '755 patent differs from the elected compound of the instant application by the following function groups: For the elected compound, M is N; Z=S(O)2; R2, which corresponds to the R1 position of claim 4 of the US '755 patent, is benzoimidazol, rather than carbazolyl, and R4, which corresponds to the R5 position of the compound of claim 4, is thienyl. However, the '015 patent teaches that, in addition to M being N, M may also be CH; Z may also be carbonyl as well as sulfonyl; and that the R5 position, which corresponds to the R4 position of the elected compound, may be occupied by a C3-7 heterocycle, or a fused aryl group (p. 3, lines 9-29, p. 4, lines 1-5, and lines 20-22, p. 5, lines 1-8, p. 7, lines 1-12). Additionally, the R1 position, which corresponds to the R2 position for the elected compound and for the formula IX compounds of the '015 publication, may be occupied by a fused aryl group (p. 3, lines 20-26, p. 7, lines 1-6). Thienyl and pyran are both C5 heterocycles, while chromene is a

fused aryl group. Carbazolyl and benzoimidazol are both fused aryl groups. Therefore, the '015 publication teaches that both the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, and the compounds of claim 4 of the US '755 patent are equivalent derivatives of each other.

43. Instant claim 30 cites the compound as stated in instant claim 23, and also, that the R2 position is occupied by a benzoimidazol group, as in the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. Claim 4 of the US '755 patent cites a compound of the formula as shown above, and in claim 4. For the compound disclosed in claim 4, the R2 position of the elected compound corresponds to the R1 position. The R1 position of the compound of claim 4 is occupied by a carbazolyl group, which may have one or more substituents (column 26, lines 38-39). While the carbazolyl and the benzoimidazol groups are not identical, they are both fused phenyl groups. The '015 publication teaches that this position, which corresponds to the R2 position for compounds of formula IX, may be occupied by fused phenyl groups, which may be substituted with one or more substituents (p. 3, lines 20-26, p. 7, lines 1-6). Therefore, the '015 publication teaches that these groups are equivalent to each other.

44. Instant claim 31 cites the compound of instant claim 23, and that the compound is selected from a list of compounds, one of which is the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-

benzoimidazol-5-yl) amide. Claim 4 of the US '755 patent cites compounds of the formula shown below, with the following functional groups:




Where M and L are CH; Z=(C=O); W=(C=O); R9, R11, and R13=H, etc.; R1=unsubstituted carbazolyl or carbazolyl substituted with one or more substituents; R2=H; R5=pyran, chromene, or benzofuran; R12=C1-8 alkyl, etc. The compound disclosed in claim 4 of the US '755 patent differs from the elected compound of the instant application by the following function groups: For the elected compound, M is N; Z=S(O)2; R2, which corresponds to the R1 position of claim 4 of the US '755 patent, is benzoimidazol, rather than carbazolyl, and R4, which corresponds to the R5 position of the compound of claim 4, is thienyl. However, the '015 patent teaches that, in addition to M being N, M may also be CH; Z may also be carbonyl as well as sulfonyl; and that the R5 position, which corresponds to the R4 position of the elected compound, may be occupied by a C3-7 heterocycle, or a fused aryl group (p. 3, lines 9-29, p. 4, lines 1-5, and lines 20-22, p. 5, lines 1-8, p. 7, lines 1-12). Additionally, the R1 position, which corresponds to the R2 position for the elected compound and for the formula IX

compounds of the '015 publication, may be occupied by a fused aryl group (p. 3, lines 20-26, p. 7, lines 1-6). Thienyl and pyran are both C5 heteroaromatic groups, while chromene is a fused aryl group. Carbazolyl and benzoimidazol are both fused aryl groups. Therefore, the '015 publication teaches that both the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, and the compounds of claim 4 of the US '755 patent are equivalent derivatives of each other.

45. Instant claim 32 cites a pharmaceutical composition comprised of the compound stated in instant claim 31, which is the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. Claim 8 of the US '755 patent cites a pharmaceutical composition comprised of the compound of claim 4. The compound as disclosed in claim 4 of the US '755 patent is equivalent to the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, in view of the '015 publication, as applied to instant claim 31 above. Therefore, claim 8 discloses that a compound which is an equivalent derivative of the elected compound is present in a pharmaceutical composition.

46. Instant claim 34 cites the pharmaceutical composition comprised of a pharmaceutically acceptable carrier and the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide. Claim 8 of the US '755 patent discloses that a compound as cited in claim 4 may be present in a pharmaceutical composition, in a pharmaceutically acceptable carrier.

The compound disclosed in claim 4 of the US '755 patent is an equivalent derivative of the elected compound, 4-octyl-1-(thiophene-2-sulfonyl)-piperazine-2-carboxylic acid (1-ethyl-2-pyridin-3-yl-1H-benzoimidazol-5-yl) amide, in view of the '015 publication, as applied to instant claim 31 above. Therefore, claim 8 discloses that a compound which is an equivalent derivative of the elected compound is present in a pharmaceutical composition, in a pharmaceutically acceptable carrier.

47. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

48. The information disclosure statements (IDS) submitted on 6/29/06 were filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is

(571)270-7710. The examiner can normally be reached on Monday-Thursday 7:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4121